IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re patent application of:
Rainer HINTSCHE *et al.*

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Examiner: SISSON, Bradley I.

For: DETECTION OF MOLECULES AND MOLECULE COMPLEXES

Supplemental Request for Reconsideration under 37 C.F.R. § 1.111

Commissioner of Patents
Washington, DC 20231

Sir:

This is in Response to the Office Action mailed March 17, 2003, for the above-captioned application, in which Examiner Sisson requested applicants to provide support for the amendments submitted January 9, 2003. A response is due on April 17, 2003. While applicant believes that no extension of time fee is due, the Commissioner is authorized to credit any overpayment or charge any deficiency to Deposit Account No. 08-1641.

Applicants herewith urge Examiner Sisson to enter the amendments previously submitted and herewith provide a copy of the amendment for reference along with a more detailed recitation of where support for such amendments can be found in the specification.

The previously submitted amendment is as follows:

23. (Amended) A method according to claim [21] 63 , wherein the measuring of the changes in current or potential is performed [are measured] using impedance spectroscopy.

24. (Amended) A method according to claim 61, wherein the changes in current or potential are measured independently of time, as a function of time or as a function of the phase angle of the current.

25. (Amended) A method according to claim [21] 63, wherein the changes in current or potential are caused by diffusion or binding of the first molecule or first molecular complex to the ultra-microelectrode array.

27. (Amended) A method according to claim [21] 63, wherein the alternating electric field comprises, is superimposed, or excited with a direct-current component.

31. (Amended) A method according to claim [21] 63, wherein the first molecule or first molecular complex binds to a binding compound on a surface of the electrode structures.

32. (Amended) A method according to claim [31] 63, wherein the first molecule or first molecular complex binds to the surface of the electrode structures via physical or chemical binding.

33. (Amended) A method according to claim [31] 63, wherein the molecule or molecular complex binds to the surface of the electrode structures via self-assembling.

34. (Amended) A method according to claim 31, wherein the first molecule or first molecular complex binds to the binding compound on the surface of the electrode structures via electropolymerization.

35. (Amended) A method according to claim [21] 63, wherein the first molecule or first [molecule] molecular complex is positioned in the gap between the electrode structures.

37. (Amended) A method according to claim 63 [21], comprising [wherein the electrode structures are layered with a substrate which is bound to an antigen or a nucleic acid molecule, said antigen or said nucleic acid molecule capable of binding to the molecule or molecular complex to be detected] a second molecule, the second molecule being selected from the group consisting of antigens and nucleic acid molecules, that binds to the first molecule or first molecular complex to be detected, wherein the second molecule is bound directly to said ultra-microelectrode array or is bound via a binding compound, and whereby the binding between the second molecule and the first molecule or first molecular complex to be detected is capable of causing the changes in current or potential between the electrode structures.

38. (Amended) A method according to claim 37, wherein the second molecule [molecular layer contacts] binds a binding compound on [with] a surface of the electrode structures.

40. (Amended) A method according to claim 37, wherein the second molecule comprises an antigen, and wherein the first molecule or [molecule] first molecular complex to be detected comprises an antibody.

42. (Amended) A method according to claim 37, wherein the second molecule comprises a first polynucleotide, and the first molecule or [molecule] first molecular complex to be detected comprises a second polynucleotide capable of binding to the first polynucleotide.

43. A method according to claim 42, wherein the second polynucleotide binds to the first polynucleotide via hybridization.

44. A method [according to claim 37, wherein the second molecule comprises a first and second polynucleotides, wherein the molecule or molecule complex to be detected comprises a third polynucleotide, and wherein the first, second and third polynucleotides are capable of forming a triple helix] of detecting a molecule or molecular complex in a sample, comprising:

(a) contacting the sample comprising a first molecule or a first molecular complex with a single ultra-microelectrode array, said ultra-microelectrode array comprising at least two electrode structures,

(b) producing an electric field between the electrode structures; and

(c) measuring changes in current or potential between the electrode structures, whereby the changes in current or potential are caused by the first molecule or the first molecular complex,

wherein said first molecule or molecular complex is a third polynucleotide that hybridizes to a second polynucleotide that is hybridized to a first polynucleotide, wherein said first polynucleotide is bound to a binding compound on said ultra-microelectrode array; and wherein each of said electrode structures is insulated from each other and is either a layer on a planar insulating support material or is incorporated in said planar insulating support material and wherein the spacing between the electrode structures is about 1 μm or less and wherein the electrode structures are arranged so closely next to one another that they approach the size of large molecule complexes.

45. (Amended) A method according to claim [21] 63, wherein the ultra-microelectrode array comprises first molecular layer and a second molecular layer, wherein the first molecular layer contacts the second molecular layer,

wherein the second molecular layer comprises a second molecule, wherein the second molecule is capable of binding to the molecule or molecular complex to be detected, and whereby the binding between the second molecule and the molecule or molecular complex to be detected is capable of causing the changes in current or potential between the electrode structures.

46. (Amended) A method according to claim [21] 63, wherein a surface of the electrode structures comprises a layer of conductive material.

47. (Canceled) A method according to claim 46, wherein the layer of conductive material comprises a noble metal.

48. (Canceled) A method according to claim 46, wherein the layer of conductive material comprises carbon materials.

49. (Canceled) A method according to claim 21, wherein the electrode structures are applied to or incorporated in an insulating material.

50. (Amended) A method according to claim [49] 63, wherein the insulating material is selected from the group consisting of silicon compounds, glass, ceramic and organic polymers.

53. (Amended) A method according to claim [52] 63, wherein the insulating material is selected from the group consisting of silicon oxides, nitrides, ceramic and plastics.

54. (Amended) A method according to claim [21] 63, wherein the electrode structures are arranged [to have] as a multi-layer structure with each layer insulated from one another.

Please add the following new claims:

63. A method of detecting a first molecule or a first molecular complex in a sample, comprising:

(a) contacting the sample comprising a first molecule or a first molecular complex with a single ultra-microelectrode array, said ultra-microelectrode array comprising at least two electrode structures;

(b) producing an electric field between the electrode structures;

(c) measuring changes in current or potential between the electrode structures, whereby the changes in current or potential are caused by the first molecule or the first molecular complex; and

(d) detecting the presence of said first molecule or first molecular complex by observing said change in current or potential;

wherein said first molecule or first molecular complex is selected from the group consisting of nucleic acids, peptides and proteins; and

wherein each of said electrode structures is insulated from each other and is either a layer on a planar insulating support material, or is incorporated in said planar insulating support material and wherein the spacing between the electrode structures is about 1 μm or less; and

wherein the electrode structures are arranged so closely next to one another that they approach the size of large molecule complexes.

64. A method according to claim 35, wherein the first molecule or first molecular complex is positioned in the gap by chemical binding, adhesion, or condensation reactions.

65. A method according to claim 37, wherein said second molecule comprises an antibody, and wherein the first molecule or first molecular complex to be detected comprises an antigen that binds to said antibody.

66. The method of either claim 63, wherein a surface of the electrode structures comprises a layer of conductive material, said material being selected from the group consisting of a noble metal, a carbon material and both a noble metal and carbon material.

67. The method of 63, wherein said ultra-microelectrode array is a noble metal or a carbon material or comprises said noble metal or carbon material.

68. The method of claim 66, wherein said noble metal is selected from the group consisting of gold, platinum and iridium.

69. The method of claim 67, wherein said noble metal is selected from the group consisting of gold, platinum and iridium.

70. A method according to claim 63, wherein each of the electrode structures is a layer sufficiently thin that the electrode layer is substantially planar.